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10/749,602	12/31/2003	Daryll A. Emery	293.00010102	8548

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EXAMINER	
LEITH, PATRICIA A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/749,602	EMERY ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/7/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-44, 67-69, 71-82, and 84 –102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-44, 67-69, 71-82, and 84 –102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/7/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

. DETAILED ACTION

Claims 34-44, 67-69, 71-82, and 84 –102 remain pending in the application and were examined on their merits. There were no claim amendments submitted by Applicants in the interim between the previous non-final Office action and this final Office action.

Rejections Removed

The following rejection has been removed due to Applicants' persuasive arguments that the combination of references does not make obvious the claimed invention:

Claims 34-44, 67-69, 71-82, and 84 –102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766) and further in view of Evans et al. (US 6,500,438 B2) in view of Genovese et al. (1998) in light of Sharma et al. (US 4458630 A)*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 37, 39-43, 67-69, 83-86, 89, 91-95 and 97-102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,538,733) in view of Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766).

Emery et al. (US 5,538,733) discussed the problem of vaccination of young animals in that maternal antibodies present in neonates may interfere with an animal's immune response, while proposing a solution of administration of vaccines

present in sustained and delayed delivery agents to young poultry between the ages of 1-90 days (see entire reference and Abstract). Emery et al. explicitly indicated that the method advantageously incorporated injection of an 'implant matrix' made of "…biocompatible, biodegradable, bioabsorbable and/or bioerodible polymeric material.." such as cholesterol and cellulosic polymers to "...release the immunogen for sustained delivery into surrounding tissue fluids over an about 1-90 day period" (see, col. 2, lines 15-55).

Emery et al. specifically indicated that "The continuous presence of a priming dose of the immunogen provides and effective way of priming a young animal so that a secondary immune response to a pathogenic infection is stimulated substantially immediately when passive protection by maternal antibodies *against the pathogen* is no longer effective" (see paragraph bridging columns 3-4, emphasis added). Hence, it is clear that Emery et al. is stating that the immunized poultry possess the maternal antibodies against the same immunogen used to inoculate the animals including domestic fowl (see also col. 9, lines 41-49).

Emery et al. indicated that the 'time-delayed implant' "…will substantially maintain integrity of the matrix for *a desired length of time*. Preferably, the matrix will remain intact for up to about 3 weeks, or after the level of maternal antibody has significantly declined, at which time the antigen is released from the matrix."

(emphasis added) Hence, the matrix is formulated for delayed delivery. Emery et al. further indicate that the matrix is formulated for delayed and sustained delivery: "The matrix may optionally be formulated to include a soluble or insoluble pore-forming agent that will dissipate from the matrix into surrounding tissue fluids causing the formation of pores and/or channels throughout the implant matrix….sodium chloride…carboxymethylcellulose" (see col. 9, lines 29-39).

A preferred immunogen for implantation disclosed by Emery et al. was siderophore receptor protein (SRP) from gram negative bacteria (see col. 7, line 50-col. 8, line 24). See also Example 2, wherein a sustained/delayed release formulation of SRP is administered to 1 day old turkey poults to establish immunity *against the SRP* indicative of an adaptive immune response. Notably, in this Example, Emery et al. specifically indicate that a further preference for delivery time to is between 1-60 days of age.

Emery et al. additionally taught the advantageous nature of administration of a booster "…to stimulate a secondary immune response in the animal," wherein the booster was an SRP. Emery et al. gave a specific example wherein a 21 day implant administered to a turkey poult is given a booster injection after the expiration of the implant, stated by Emery et al. to be 21 days after implantation, at about 28-48 days to stimulate the immune response (see col. 11, lines 1-19). This booster time

disclosed by Emery et al. falls completely within the claimed booster time of 3-12 weeks (equates to 21-84 days). Serological profiles to quantify antibody titers to SRP were known at the time of Emery et al. and specifically discussed (see col. 11, lines 33-58).

Emery et al. did not specifically teach wherein the siderophore receptor was administered *in-ovo* at 'a time when maternal antibodies of the bird to the immunogen are sufficiently reduced'. Nor did Emery et al. teach the specific injection times as found in claims 39-42 and 44 or wherein a second dose of immunogen was given at 3-12 weeks post-hatching (claim 43). Emery et al. further did not teach the incorporation of porins into their vaccine.

Emery et al. (US 5,830,479) disclosed a method for immunizing poultry with a siderophore from gram-negative bacteria wherein the siderophore is enterochelin or siderophore citrate as examples (col.s 1-53, particularly col. 5, lines 29-38 and claims 1 and 3). As stated by Emery et al. "The vaccine of the present invention may be used for preventing and eliminating infections of gram-negative bacteria in poultry and other animals including humans" (col. 11, lines 9-12). Emery et al. specifically suggested sustained release administration of the vaccine (col. 11, line 15) and *in-ovo* administration in poultry: "The vaccine of the present invention may be used for

preventing and eliminating infections of gram-negative bacteria in poultry and other animals, including humans….may be delivered to the animal, for example, by…egg inoculation (i.e., poultry…by known techniques in the art…the vaccine contains an amount of a siderophore receptor protein to stimulate a level of active immunity in the animal to inhibit and/or eliminate gram-negative bacterial pathogenesis and/or sepsis" (col. 11, lines 10-21). Emery et al. specifically taught that "The protein may also be incorporated into a carrier which is a [*sic*] biocompatible and can incorporate the protein and provide for its controlled release or delivery, for example, a sustained release polymer such as a hydrogel, acrylate, polylactide, polycaprolactone, polyglycolide or copolymer thereof…an example of a solid matrix for implantation into the animal and sustained release of the protein antigen into the body is a matabolizable matrix, as described…in US …4,452,775 (Kent)" (col. 11, lines 27-36). Emery et al. also taught the advantageous use of a booster vaccine given "21-28 days after the first injection" and the use of adjuvants such as porins from gram negative bacteria for administration along with SRP's (see, col. 7, line 50-col. 8, line 9). Emery et al. offered that the amount of vaccine was varied in order to achieve optimal vaccination (see col. 11, line 49- col. 12, line 6).

Phelps et al. (US 5, 339,766) disclosed a method for introducing mat6erinl into poultry eggs during early embryonic development which included injection of a therapeutic substance contained within a biodegradable matrix such as polylactide

polymers (lactides/glycolides) directly into the developing bird egg. Materials intended for delivery included "vaccines, vitamins, antibiotics hormones, enzyme inhibitors, peptides, cells, DNA and other therapeutic molecules" (col. 3, lines 33-36). Phelps et al. discussed that, "Eggs treated by the method of the present invention are preferably fertile eggs which may be in any period of incubation, from early to late… " (col. 4, lines 15-18). Phelps et al. further explained that "Such beneficial effects included increased growth, disease resistance due to in ovo vaccination, increased percentage hatch of multiple incubated eggs, and otherwise improved physical characteristics of hatched poultry" (col. 1, lines 20-24).

One of ordinary skill in the art would have been motivated to administer a sustained-release formulation *in ovo*, to a bird (i.e., poultry such as chicken) wherein the formulation comprised a siderophore receptor such as enterochelin, and wherein the sustained-release formulation was sustained until the hatching of the bird (i.e., 1-60 or 1-90 days post-hatching) in order to increase the bird's immune system to foreign disease causing bacteria. It was clear from the prior art that siderophore receptors from gram-negative bacteria were known to vaccinate birds, and suggested for use *in-ovo* by Emery et al. '479. Further disclosed by Emery et al. as well as Phelps et al. were suitable mediums and sustained release biocompatible matrices for *in-ovo* injection of vaccines. The ordinary artisan would have recognized, in view of Emery '773 that sustained release of SRPs to young poultry or poultry embryos (in-ovo) would need to be formulated to release the SRPs at a time that the immunogen is "sufficiently reduced

so that the birds are capable of mounting an adaptive immune response". This knowledge in the art of poultry immunization is made perfectly clear by Emery '773 and is not considered a novel idea. It is clear from the teachings of the references as a whole, that the Emery et al. patent '773 although not teaching egg inoculation of their sustained/delayed release matrix SRP vaccine is cured by the subsequent Emery '479 patent which clearly suggests that the same matrix, including SRP and advantageously the addition of porin as an adjuvant, into an egg to vaccinate young poultry.

In-ovo vaccination techniques as claimed were known and well-utilized and rendered obvious at the time the Invention was made as evidenced by Phelps et al. Emery et al. '773 and Emery et al. '749 together taught optimal times for vaccinating young poultry at a time when maternal antibodies were reduced in order for the bird to mount an immune response; Emery et al. '773 teaching specifically times advantageous to administer such a vaccine which included SRP when maternal antibodies to SRP were 'sufficiently reduced': the 'time-delayed implant' "…will substantially maintain integrity of the matrix for *a desired length of time*. Preferably, the matrix will remain intact for up to about 3 weeks, or after the level of maternal antibody has significantly declined, at which time the antigen is released from the matrix." It is the opinion of the Examiner that at the time the invention was made, the claimed invention was well-within the purview of the ordinary artisan. Time delayed/sustained matrices for delivering SRP to poultry were known in the art at the time the invention was made and known to be manipulated to release SRP at a desired time. Clearly, the results

achieved by both Emery et al. patents include successful vaccination of young poults anywhere from injection at one day (with the sustained delivery matrix of Emery et al. '773), three weeks (see Example 3, Emery et al. '479), six weeks (Emery et al. '479).

Clearly, there is no explicit time indicated in the prior art nor the Instant specification of 'until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an adaptive immune response to the immunogen' because this time would vary from bird to bird. Hence the reason for the delayed/sustained release formulations of both Emery et al. patents. Such a formulation intended for sustained/delayed release would provide continual vaccine delivery over a desired amount of time in order to successfully vaccinate young birds.

Claims 34-44, 67-69, 71-82, and 84 –102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766) in view of Emery et al. (US 5,538,733).and further in view of Evans et al. (US 6,500,438 B2).

The teachings of Emery et al. '749, Emery et al. '773 and Phelps '776, were discussed *supra*. None of these references specifically taught t the specific injection protocols as recited in claims 35, 36, 38 and 44.

Evans et al. (US 6,500,438 B2) taught a method for *in ovo* vaccination of chickens with *E. sporozoites* via injection, wherein the injection was preferentially performed in the final quarter of incubation or specifically at day 18 of incubation, however would have been effective during any time of incubation (col. 2, lines 1-6, col. 3 lines 25-27 and Example 1).

Hence, although the prior art did not teach a specific embodiment where SRP was injected into bird eggs at the claimed injection times as required by claims 35, 36, 38 and 44, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. It is clear from the prior art teachings as a whole that the sustained release matrices including SRP and advantageously including porins as an adjuvant to the SRP vaccine were formulated to release during a time that maternal antibodies to the vaccine were sufficiently reduced in order for the chick to produce antibodies to the vaccine. Such matrices were well-known in the art and producing such compositions was within the skill level of the ordinary artisan at the time the invention was made. In-ovo injections to produce an immune response were further known in the prior art to be carried out within the time frames specified by the claims. There is no one limitation within the claims which is deemed to be directed toward a novel invention; as the prior art provides a clear roadmap to the claimed invention.

The Supreme court has acknowledged:

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. **If a person of ordinary skill can implement a predictable varition..103 likely bars its patentability**…if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions…
>
> …**the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results** (see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007) emphasis added.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments concerning these remaining rejections as set forth *supra* were very carefully considered; however, were not found to be convincing to obviate said rejections.

Applicants first argue:

> Immune tolerance to a foreign antigen can occur when a subject is exposed to a foreign antigen under conditions that elicit specific unresponsiveness to the foreign antigen rather than an adaptive humoral immune response to the antigen. In other words, under some circumstances, exposure to a foreign antigen does not necessarily result in the challenged subject mounting an adaptive immune response, but instead results in the subject's immune system perceiving the foreign antigen as "self" and establishing antigen-specific immune non-response.
> Many of the conditions under which immune tolerance may be induced are present in the circumstance of in ovo vaccination as recited in Applicants' claims. (See, Microbiology, fourth edition, Davis et al. eds., 1990, J.B. Lippincott Co., Philadelphia, Pennsylvania, pp. 381-382.) For example, SRPs-the immunogens specifically identified in the Office Action-are monomeric antigens, not aggregated; sustained release implants are not equivalent to injection into tissue, but are more similar to intravenous administration; and in ovo administration necessarily results in vaccination of the embryo rather than adult. So, one skilled in the art would recognize that vaccinating embryos or newly-hatched chicks using sustained release implants harbor the risk of inducing immune tolerance to the immunogen in the vaccine rather than raising adaptive immunity against the immunogen. Many of these conditions are present whether the sustained release implant is administered at one day of age (as in the '733 patent) or in ovo, as in the present claims (pp. 7-8 Remarks).

However, Applicants' arguments regarding the fact that an immune response to the antigen may not have occurred due to *in-ovo* vaccination of chicks using sustained release would be an exception to the rule and is not a persuasive argument. The skilled artisan would have understood at the time the invention was made that vaccinations are not 100% successful. Based upon the combined teachings of the prior art, the ordinary artisan would have had a reasonable expectation of success; the prior art already recognized the use of SRPs for vaccination into poults as well as in-ovo via use of sustained delivery matricies. It is evident upon reading the references in combination; that the ordinary artisan, considering the successfulness of vaccination using SRP proteins in young chicks, that delivery of SRP's comprising a delayed release matrix, which was already taught by the prior art, to release at times already known to be

successful for vaccinating young birds would have been prima facie obvious at the time the invention was made. There is no indication in the Specification that Applicants' have achieved any unexpected result over what was already clearly suggested by the combination of the prior art teachings and hence, absent such an unexpected result, the claimed invention is deemed an obvious combination of prior art elements.

Applicants argue:

> The difference between vaccinating an egg by sustained release of a selected immunogen from a biocompatible implant at one day of age versus injecting the biocompatible implant in ovo-and a compelling reason why one skilled in the art would not extend the teaching of the '733 patent to in ovo delivery-is that *the risk of inducing immune .tolerance to the immunogen is greater when the biocompatible implant containing the immunogen is delivered in ovo compared to delivering the biocompatible implant after hatch. One reason for the increased risk of inducing immune tolerance when the biocompatible implant is injected in ovo is the different amounts of-and the corresponding effects of the different amounts of-circulating maternal antibody in the embryo versus in the newly-hatched chick.*
> Each of claims 34, 69, and 84 recites that the egg (or eggs) into which the biocompatible implant is injected comprises maternal antibody to the selected immunogen. Prior to hatch, some of the maternal antibody circulates in the embryo but most remains sequestered in the yolk. At hatching, however, the yolk is fully absorbed and the maternal antibody from the yolk is fully absorbed into the circulation of the chick. Thus, the chick-but not the embryo-has the full passive immunization benefit of the maternal antibodies. Consequently, the circulating maternal antibody environment is very different in the embryo than in the newly-hatched chick and this difference influences the risk of inducing immune tolerance. (p. 8, Remarks, emphasis added).

However, Applicants' assertions are unsubstantiated and found unpersuasive in view of the prior art teachings. Emery '733 explicitly taught *in-ovo* vaccination using sustained/delayed release of SRP antigen to vaccinate poultry. Although there is no specific example of where Emery performed *in-ovo*

vaccination; there is an explicit suggestion for the ordinary artisan to perform *in-ovo* vaccination by Emery et al. and further, *in-ovo* vaccination techniques were well-known and conventional in the art at the time the Invention was made. While Applicants point to unknown parameters and unpredictability with regard to *in-ovo* vaccination, the level of unpredictability in the Instant case does not rise to the level of patentability considering that the prior art explicitly suggested *in-ovo* vaccination of birds, specifically taught the delayed/sustained release times of the claims and specifically taught the use of SRP proteins for these purposes. The only teaching lacking between the two Emery et al. patents and the claimed invention is the age of the egg at vaccination. However, vaccination at this time was known in the art as disclosed by Evans et al. It is deemed, in light of the combination of prior art references; that the ordinary artisan, having the knowledge that SRP proteins were advantageously administered to young poultry to vaccinate them against harmful bacteria, that SRP proteins were advantageously formulated to be delivered by sustained/delayed release until a time when 'maternal antibodies...are reduced so that the bird is capable of mounting an adaptive immune response,' that SRP proteins were specifically suggested to be delivered *in-ovo* with sustained release, that the claimed times for release of the SRP were known in the art and that *in-ovo* vaccination techniques were also well-known in the art (Phelps et al.), and vaccination at the times as indicated by the claims were also known in the art (Evans et al.).

Thus, absent any evidence of an unexpected result, the claimed invention is deemed an obvious method already suggested by the prior art teachings. The ordinary artisan, relying on the above-cited US Patents would have had a reasonable expectation of success in producing the claimed method. Although neither Emery et al. patents explicitly demonstrated *in-ovo* vaccination of SRP proteins at the age of the egg as indicated by claims 35 and 36 for example, determining a time to vaccinate poultry eggs with known vaccines such as SRPs which were already known to be delivered in delayed/sustained release matricies at the times as required by the claims is deemed well-within the skill level of the ordinary artisan and would have been achieved through routine optimization/experimentation. The Specification as a whole appears to be solving an asserted problem of delivering an SRP protein to a young poult in such a manner as to deliver said SRP at a time when maternal antibodies are reduced. However, it appears that the problems asserted by the Specification *were already solved by the teachings of the prior art US Patents*. There is nowhere in the Specification which suggests that the time of vaccination is particularly crucial or where these times were found to achieve a superior result. The prior art as well as the claims teach a broad window for sustained/delayed release of the SRP antigen to deliver to a poultry; this is because it appears that there is no absolute time which is known when maternal antibodies will be at the lowest level to ensure maximum protection since this time would vary from bird to bird. Absent such additional information which would demonstrate that

Applicants have achieved a result which was not already found predictable based upon the combination of the prior art teachings; it is decidedly taken that the vaccination times were an obvious choice based upon the consideration that eggs were routinely vaccinated at these times. Hence, Applicants' arguments as presented on page 9 of their remarks concerning day old chicks and the amount of maternal antibody are unpersuasive. Applicants are claiming a method which was already suggested by the prior art; the maternal antibody titers of the chicks were not measured in Applicants data present in the Specification; it is unknown exactly when the maternal antibodies to an SRP protein will be sufficiently low to amount a maximum immune response; however, the prior art already recognized that SRPs could be delivered via sustained/delayed matricies in order to release the SRP proteins within a broad window to achieve a desired immune result (i.e., vaccination). It does not appear that Applicants have gone above-and-beyond what was already known and expected from SRP vaccination of poultry as disclosed by the prior art.

Applicants' arguments regarding that when a biocompatible implant is provided *in ovo*, the level of maternal antibody absorbed by the chick…at day 20 of incubation…is incomplete, and as a consequence, the embryo is at risk for developing immune tolerance (p. 9, Remarks) is not found convincing. The prior art already recognized that the presence of maternal antibodies in young poultry hastened the need for delivery of vaccines at a time when maternal antibodies in

the poultry were reduced (both Emery et al. US Patents). Additionally, these statements are not provided in the Specification, and there is no evidence given in the Specification that the time chosen for vaccinating the eggs was significant. Absent such indication; seeing that the prior art already specifically suggested *in-ovo* vaccination with SRP proteins using biocompatible implants which provide for sustained/delayed release for the same delivery times as required by the claims, Applicants' age of egg to be vaccinated as claimed is deemed obvious since these were well-known times to vaccinate chicks *in-ovo*. Considering that the prior art already taught that the biocompatible matrix could have been formulated to release implant "….for *a desired length of time*. Preferably, the matrix will remain intact for up to about 3 weeks, or after the level of maternal antibody has significantly declined, at which time the antigen is released from the matrix" (Emery et al., 479, see citation above) the ordinary artisan would have had a reasonable expectation of success in carrying out the claimed method.

Applicants' arguments regarding the embryo's immune system and Applicants' statements that the effect of administering the sustained release implant to an embryo is unpredictable is not found convincing. While there is an acceptable amount of unpredictability regarding the immune functions of poultry embryos, if there were unpredictability in the art regarding this immunity, the unpredictability still exists in this application because there is no indication in the Instant specification that Applicants' have achieved any result which was not

already expected by the prior art. Applicants' only example regarding *in-ovo* inoculation merely quantitated live births and evaluated the injection sites. Applicants did not state exactly how the biocompatible matrix was prepared for this example (i.e., a determined release time), did not measure the maternal antibody titers of the eggs, did not measure antibody titers of the chicks after hatching and thus did not evaluate the overall success of a 20 day old egg vaccination. Nor did Applicants provide any comparative data which would demonstrate that an egg at day 20 of incubation would provide for any result which would not be expected by the prior art (i.e., vaccination). It appears that this example, Example 4 in the Specification; the only example in the Specification pertaining to *in-ovo* vaccination; was set forth to assess the toxic nature of the injection itself, as there is no subsequent data at all concerning these inoculated eggs. Hence, even considering if there is unpredictability in the art with regard to vaccination of poultry eggs 1) the prior art suggested *in-ovo* vaccination of SRP proteins using sustained/delayed release matricies, 2) the prior art taught the advantageous nature of delivering SRP proteins in biocompatible sustained/delayed release matricies to deliver SRP proteins to poults when decreased maternal antibodies were present and 3) *in-ovo* vaccinations were routine in the art and 4) *in ovo* vaccinations were successfully achieved by injecting antigens at the times recited by the claims. Hence, if the Examiner had reason to believe that the claimed composition was unpredictable, the claims themselves would be rejected under 35 USC 112 First paragraph,

because if a large degree of unpredictability existed, Applicants' specification would not cure this deficiency considering the lack of teachings in the Specification with regard to in-ovo inoculation. Nevertheless, it is taken from the prior art as a whole that the claims are enabled because the prior art already taught successful vaccination of young poultry with SRP proteins via use of a biocompatible matrix designed to provide sustained/delayed release until a time when maternal antibodies were sufficiently reduced so the bird could mount an immune response to the immunogen (SRPs) and because SRPs delivered in such matricies were specifically suggested for in-ovo administration. Considering the breadth of information concerning poultry vaccination with SRPs, the prior art is deemed enabling and the artisan would have had a reasonable expectation of success in carrying out the claimed invention.

Applicants' argue:

> As explained by Dr. Emery during the interview, the methods recited in claims 34, 69, and 84 permit those in the poultry industry to vaccinate a generation of eggs, at one time, and ensure that the resulting chicks can raise an adaptive immune response against a selected immunogen at the time-which can vary from egg to egg in a single generation from a single hen-when maternal antibody to the selected immunogen wanes. In the absence of such sustained release vaccination methods, those in the industry must otherwise vaccinated each chick every day over a multi-week period to ensure protection for the entire new generation because the waning of maternal antibody, if ever present at all, can vary from chick to chick. (p. 10, Remarks).

The Examiner does not disagree to the statement that "…claims 34, 69, and 84 permit those in the poultry industry to vaccinate a generation of eggs, at one

time, and ensure that the resulting chicks can raise an adaptive immune response against a selected immunogen at the time-which can vary from egg to egg in a single generation from a single hen-when maternal antibody to the selected immunogen wanes." However, the *combination of the prior art already taught this information* and the ordinary artisan, having the above-cited references before him or her would have had a reasonable expectation of success in carrying out the claimed invention based upon those teachings.

[If]… there are [a] finite number of identified, predictable solutions, [a] person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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